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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,723	10/11/2005	Veronique Coxam	P70904USD	6839
136 7590 10/01/2009 JACOBSON HOLMAN PLLC 400 SEVENTH STREET N.W. SUITE 600 WASHINGTON, DC 20004				
EXAMINER				
FRAZIER, BARBARA S				
ART UNIT		PAPER NUMBER		
1611				
MAIL DATE		DELIVERY MODE		
10/01/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/552,723

Applicant(s)

COXAM ET AL.

Examiner

BARBARA FRAZIER

Art Unit

1611

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 3, 6, 15, 17, 20 and 24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4, 5, 7-14, 16, 18, 19, 21-23, 25 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of Claims

1. Claims 1-26 are pending in this application.
2. Claims 3, 15, 17, and 24 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/8/08.
3. Claims 6 and 20 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/8/08.
4. Claims 1, 2, 4, 5, 7-14, 16, 18, 19, 21-23, 25, and 26 are examined.

Claim Rejections - 35 USC § 103

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
6. **Claims 1, 2, 4, 5, 7-14, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockwood (US Patent 7,445,807), as evidenced by Nachman (US Patent 5,714,150).**

The claimed invention is drawn to a method for inhibiting bone resorption in humans or animals comprising the administration to a subject in need thereof a

composition comprising oleuropein (see claim 1). Applicants have elected osteoporosis as the disease to be treated (see claim 7).

Lockwood teaches agglomerated granular protein-rich nutritional supplements, for use by specific groups of individuals (abstract). Lockwood teaches that one group to be treated include postmenopausal women, who are particularly susceptible to osteoporosis (col. 1, lines 35-38), and teaches supplements designed for women (columns 13 and 14). The supplements may comprise edible plant extracts, including olive leaf extract (col. 9, lines 28-37). Olive leaf extract is known to inherently contain oleuropein; as evidence, Nachman teaches a method of producing olive leaf extract known as oleuropein with valuable medicinal properties (see abstract and column 1). Therefore, one skilled in the art of edible plant extracts would envisage oleuropein from the disclosure of "olive leaf extract" in Lockwood.

Lockwood does not specifically teach that the supplement comprising olive leaf extract inhibits bone resorption.

However, it would have been obvious to a person having ordinary skill in the art at the time the invention was made to use the supplement taught by Lockwood to treat bone resorption; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because Lockwood fairly teaches and suggests supplements for women, including women susceptible to osteoporosis, and Lockwood also fairly teaches and suggests the incorporation of edible plant extracts, including olive leaf extract, in said supplements. Thus, one skilled in the art would be motivated to select the use of olive leaf extract in the supplement for women by routine experimentation, in order to

optimize the intended use of the resulting supplement, which includes making women less susceptible to osteoporosis, thereby inhibiting bone resorption.

Regarding claim 2, Lockwood teaches that the supplement is in oral unit dosage form (abstract).

Regarding claims 4, 5, and 7, Lockwood teaches that the supplements may be used for postmenopausal women which are particularly susceptible to osteoporosis (col. 1, lines 35-38); said women would naturally seek to prevent bone disorders, including bone loss which occurs with aging and disorders associated with unbalanced bone formation-bone resorption ratio. Said women also might suffer from type I or type II osteoporosis or secondary osteoporosis.

Regarding claims 8 and 9, Lockwood teaches that the supplement may be in the form of a rapidly dissolvable wafer or dissolved in a liquid (column 19); said forms reasonably read on "a food composition or beverage" in wet or dry form.

Regarding claims 10-13, Lockwood teaches that the extract may be from olive leaf (i.e., *olea europaea*).

Regarding claim 14, Lockwood teaches that the supplements for women may comprise 50 mg of edible plant extracts (col. 14, line 32). While Lockwood does not explicitly state that the supplements are administered daily, Lockwood does teach that certain components are formulated according to the Recommended Daily Allowance (for example, see col. 9, lines 5-10), and therefore one skilled in the art would reasonably expect that the supplements are administered daily.

Regarding claims 25 and 26, Lockwood teaches that the supplement may be in the form of a rapidly dissolvable wafer, including a combination of carbohydrate and non-caloric sugar substitute (col. 19, lines 21-26). Said form reasonably reads on "confectionary product" and "cookie".

Response to Arguments

7. Applicant's arguments filed 6/24/09 have been fully considered but they are not persuasive.

Applicants argue that Lockwood provides many examples of nutritional supplements, one of which is specifically designed for women, and another one of which is specifically designed for older adults. Applicants argue that the nutritional supplement for women comprises edible plant extracts, but does not describe the use of olive leaf extract, and that the nutritional supplement for older adults does not comprise any edible plant extracts.

This argument is not persuasive because Lockwood fairly teaches and suggests that olive leaf extract is a suitable plant extract in its nutritional supplements (col. 9, lines 28-37). While Lockwood does describe plant extracts which are preferred in its nutritional supplements for women, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

In response to Applicant's arguments regarding the Nachman reference (page 4 of Applicant's remarks), specifically, that Nachman does not teach that oleuropein might be used to stimulate bone formation and/or inhibit boneresorption and/or treat

osteoporosis, this argument is not persuasive because the teachings of Nachman are relied upon only to demonstrate that olive leaf extract is known to comprise oleuropein, and therefore one skilled in the art would envisage oleuropein from the disclosure of "olive leaf extract" in Lockwood.

Applicants also argue that there is no indication that the nutritional supplement for women is designed for young or older women, or whether it is designed for pre- or postmenopausal women. Applicants argue that the extensive list of preferred edible plant extracts suitable for use in the nutritional supplement for women does not include olive leaf extracts, and therefore Lockwood does not teach or suggest the use of including olive leaf extracts in nutritional supplements for women.

This argument is not persuasive because Lockwood fairly teaches and suggests that olive leaf extract is a suitable plant extract in its nutritional supplements (col. 9, lines 28-37). While Lockwood does describe plant extracts which are preferred in its nutritional supplements for women, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). Furthermore, one skilled in the art would reasonably expect that the nutritional supplements for women would be suitable for older (postmenopausal) women, since the nutritional needs of postmenopausal women are mentioned by Lockwood in the context of the nutritional and health needs of women in general (col. 1, lines 30-37).

In response to Applicant's arguments that nothing in Lockwood teaches or suggests that olive leaf extracts are helpful for treating osteoporosis, it is noted that

Applicant's claims are not limited to methods wherein the active agent treating osteoporosis is oleuropein; rather, the claims merely require that a composition comprising oleuropein is used to stimulate bone formation and/or inhibit bone resorption. Applicant's use of the open-ended term "comprising" allows for the presence of other compounds, including those which are useful for treating osteoporosis, to be present in the composition.

Therefore, it is the Examiner's opinion that the claims are rendered obvious.

8. Claims 1, 16, 18, 19, and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamdi et al (US 2003/0004117) in view of Katori et al (Inflamm. Res. 49 (2000), pp. 367-392).

The claimed invention is delineated above (see paragraph 6).

Hamdi et al teach methods for inhibiting angiogenesis comprising administering oleuropein and/or the products of its hydrolysis in therapeutically effective amounts; said methods may be utilized to treat a wide variety of inflammatory conditions (abstract).

Hamdi et al do not specifically teach administering oleuropein or a derivative thereof to inhibit bone resorption.

Katori et al teach that COX-2 has been reported in several pathophysiological states, including angiogenesis and bone absorption (abstract).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to use oleuropein to inhibit bone resorption; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the

skilled artisan would reasonably expect that compounds known to inhibit one pathophysiological state in which COX-2 is present (i.e., angiogenesis, as taught by Hamdi et al) would also inhibit another pathophysiological state in which COX-2 is present (i.e., bone resorption, as taught by Katori et al). Furthermore, the populations of subjects with angiogenesis and bone resorption are not mutually exclusive, i.e., one would reasonably expect at least a portion of those with angiogenesis would also suffer bone loss. Therefore, one skilled in the art would reasonably expect that, when oleuropein is administered to inhibit angiogenesis, bone resorption is also inhibited.

Regarding claim 16, Hamdi et al teach that a pharmaceutical composition of oleuropein may be administered (paragraph 15).

Regarding claims 18, 19, and 21, Hamdi et al teach that a disease that can be treated by administration of oleuropein is rheumatoid arthritis (paragraph 67). One skilled in the art would reasonably expect that said subjects would also seek to prevent bone loss that occurs with aging and/or a pathology associated with an unbalanced bone formation-bone resorption ratio and/or might suffer from osteoporosis.

Regarding claim 22, Hamdi et al teach that the compositions may be in a suitable form for oral, parenteral, intraperitoneal, or intradermal administration (paragraph 74).

Regarding claim 23, Hamdi et al teach that the compositions may be administered orally (paragraph 74) in an amount of approximately 0.030 g to 20 g (i.e., 30-20,000 mg). This amount overlaps that of the claimed invention, and one skilled in the art would be motivated to manipulate the amount of oleuropein from within said

ranges by routine experimentation, in order to optimize the therapeutic effect of the resultant composition.

Response to Arguments

9. Applicant's arguments filed 6/24/09 have been fully considered but they are not persuasive.

Applicants argue that a person of skill in the art seeking to treat osteoporosis would not look to Hamdi, which mentions "a plethora of health conditions", but is silent with respect to the treatment of osteoporosis.

This argument is not persuasive because the rejection is not based on the teaching of Hamdi alone, but rather Hamdi in view of Katori, which teaches that COX-2 has been reported in several pathophysiological states, including angiogenesis and bone absorption. Therefore, one skilled in the art would reasonably expect that compounds known to inhibit one pathophysiological state in which COX-2 is present (angiogenesis) would also inhibit another pathophysiological state in which COX-2 is present (bone resorption). Thus, one skilled in the art would find it obvious to try the composition of Hamdi for inhibiting bone absorption, with a reasonable expectation of success.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does

not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to Applicant's arguments that both bone absorption and angiogenesis are complex phenomena, and reliance on the articles of Shen et al and Clarke et al (page 8 of Applicant's Remarks), it is noted said documents have not submitted by Applicants, and therefore have not been considered.

In response to Applicant's arguments that Katori teaches that COX-2 is involved in many other phenomena than bone adsorption, and that angiogenesis is therefore only one particular state in which COX-2 is involved, amongst many others, it is noted that Katori still fairly teaches and suggests that COX-2 is involved in both angiogenesis and bone absorption; therefore, one skilled in the art would reasonably expect that a composition useful for inhibiting angiogenesis (i.e., the composition of Hamdi) would also be useful for inhibiting bone absorption, absent evidence to the contrary.

Conclusion

No claims are allowed at this time.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611